16837 Multivalent bacterial inhibitor protects against toxins

16843 Chip off the old block

17023 Horizontal gene transfer "invaders"

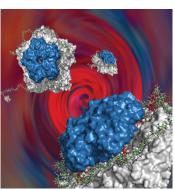
17046 Prenatal famine linked to genetic changes

17139 Vasopressin regulates maternal behaviors

CHEMISTRY, MICROBIOLOGY

Multivalent bacterial inhibitor protects against toxins

Certain bacteria, such as enterohemorrhagic Escherichia coli O157:H7, are difficult to treat because destruction of the cells by standard antibiotics releases bacterial toxins. Pavel Kitov et al. have created a class of multivalent inhibitors that can bind



Shiga toxin produced by E. coli O157:H7 and HuSAP component.

and sequester such toxins through multiple, low-affinity interactions. The authors designed a polymer scaffold that aggregated the E. coli Shiga toxin and a circulating plasma protein, human serum amyloid P (HuSAP), which is a component of the innate immune system. Both the toxin and the immune protein bind their respective ligands—the Pktrisaccharide and cyclic pyruvate ketal, respectivelyextremely weakly. The authors

arranged these ligands precisely on the scaffold to achieve sufficient binding of the target toxins and neutralization of immune proteins. The inhibitor, termed (S)-PolyBAIT, protected mice expressing HuSAP from the effects of a toxic dose of the Shiga toxin, which causes hemolytic-uremic syndrome. (S)-PolyBAIT promoted the formation of stable toxin-HuSAP complexes and directed them for disposal in the reticuloendothelial system. This class of inhibitors, used in conjunction with standard antibiotics, could be an effective therapy for many types of bacteria that produce soluble toxins, the authors say. — F.A.

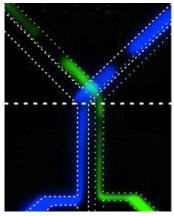
"In vivo supramolecular templating enhances the activity of multivalent ligands: A potential therapeutic against the Escherichia coli O157 AB₅ toxins" by Pavel I. Kitov, George L. Mulvey, Thomas P. Griener, Tomasz Lipinski, Dmitry Solomon, Eugenia Paszkiewicz, Jared M. Jacobson, Joanna M. Sadowska, Missao Suzuki, Ken-ichi Yamamura, Glen D. Armstrong, and David R. Bundle (see pages 16837–16842)

CHEMISTRY

Chip off the old block

Biological cells typically rely on small signaling molecules to send and receive information. Without an optical or electrical probe, studying the dynamics of such systems has been virtually impossible because of an inability to design a device to deliver, capture, and interpret these signals. To help solve this

problem, Delai Chen et al. created the "chemistrode," a microfluidic chip analogous to an electrode that enables researchers to record molecular signals with a high temporal and spatial resolution. To deliver and capture molecular signals, the lab-on-a-chip uses plug-based multiphase microfluidics surrounded in a fluorocarbon carrier fluid to avoid losing the signals as they move into the chambers of the chip. The chemistrode was fabricated using multilayer soft lithography, and



The microfluidic "chemistrode."

can detect insulin secretion from a single murine islet, providing a time-resolved chemical record of a system's response to stimulation. Although they note that further testing is necessary to determine the chemistrode's usefulness, Chen et al. anticipate that the device will eventually be a practical tool to probe the local dynamics of chemically responsive matter in chemistry and biology, such as bacterial biofilms, neural and glial networks, hormonal signaling, and other systems relying on extracellular signaling. — C.A.

"The chemistrode: A droplet-based microfluidic device for stimulation and recording with high temporal, spatial, and chemical resolution" by Delai Chen, Wenbin Du, Ying Liu, Weishan Liu, Andrey Kuznetsov, Felipe E. Mendez, Louis H. Philipson, and Rustem F. Ismagilov (see pages 16843–16848)

EVOLUTION

Horizontal gene transfer "invaders"

In most eukaryotic cells, genes are inherited or passed along from parent to offspring. Lateral or horizontal transfer of genetic information, however, is central to the evolution of



Six tetrapod species whose lineages were colonized by a DNA transposon of the hAT superfamily.

simple prokaryotes. Horizontal transfer occurs when exogenous genetic elements, delivered by viruses, plasmids, or transposons, incorporate themselves into a host genome. John Pace et al. identified mobile genetic elements that were acquired by horizontal transfer instead of by traditional inheritance in several mammalian and nonmammalian tetrapod species. While surveying DNA transposons in the bushbaby (Otolemur garnettii), a prosimian primate, the authors

identified previously uncharacterized elements of the hAT(hobo/Activator/Tam3) transposon superfamily, which they termed Space Invaders (SPIN). Upon searching nucleotide databases, they found SPIN in five additional mammalian species, including brown bats, rats and mice, and tenrecs and opossums, as well as in the green anole lizard and the African clawed frog. SPIN was not present in the genomes of many other vertebrate species. This patchy distribution, the high level of sequence identity (>95%) despite hundreds of millions of years of divergence between these species, and the lack of selection acting to preserve the integrity of these sequences indicated that SPIN likely propagated by horizontal transfer. These germline infiltrations, the authors say, occurred ≈15-46 million years ago and fueled evolutionary innovation. — F.A.

"Repeated horizontal transfer of a DNA transposon in mammals and other tetrapods" by John K. Pace II, Clément Gilbert, Marlena S. Clark, and Cédric Feschotte (see pages 17023–17028)

GENETICS

Prenatal famine linked to genetic changes

Studying a cohort of children born during the wartime food embargo in the Netherlands in 1944, Bastiaan Heijmans et al. show that prenatal famine is associated with changes to the insulin-like growth factor II (IGF-2) gene that can persist into midlife. The authors found hypomethylation in the IGF-2 gene in children conceived during the famine, who are now middle-aged adults, when compared with their same-sex siblings. Those persons exposed to the famine during the last 10 weeks before birth did not show any differences in IGF-2 methylation, indicating that these changes occurred very early in development. The wellcharacterized IGF-2 gene is maternally imprinted and primarily affects growth and development during gestation. Although hypomethylation of IGF-2 into midlife demonstrates that early prenatal environment can cause lifelong epigenetic changes, Heijmans et al. suggest that further studies are needed to determine whether such changes to IGF-2 cause other phenotypic changes. — C.A.



B17 Flying Fortress dropping food over the Western Netherlands for famine relief in May 1945. (Source: **U.S. National Archives)**

"Persistent epigenetic differences associated with prenatal exposure to famine in humans" by Bastiaan T. Heijmans, Elmar W. Tobi, Aryeh D. Stein, Hein Putter, Gerard J. Blauw, Ezra S. Susser, P. Eline Slagboom, and L. H. Lumey (see pages 17046–17049)

NEUROSCIENCE

Vasopressin regulates maternal behaviors

Despite its similarity to oxytocin, a mammalian hormone associated with breast-feeding and maternal behavior, vasopressin has not been previously linked to maternal behaviors.

Oliver Bosch and Inga Newmann found that brain vasopressin, a neuropeptide associated with directing social behavior, plays a key role in regulating maternal behaviors. The authors show that blocking the vasopressin V1a receptor via intracerebroventricular (ICV) administration of a V1a antagonist signifi-



Vasopressin-treated rats show reduced maternal behavior.

cantly diminished several maternal behaviors in rats, such as arched back nursing and direct pup contact. Long-term ICV administration of vasopressin, as well as genetically up-regulating V1a receptors by using an adenoviral vector, increased maternal behavior, whereas an infusion of vasopressin V1a receptor antisense oligodeoxynucleotides in the medial preoptic area impaired maternal behaviors, including pup retrieval. The authors also found that treatment-induced impairment of vasopressin-mediated maternal behavior increased adult emotionality and impaired social interactions in male offspring. Bosch and Neumann show that rats bred for high anxietycharacterized by genetically determined high levels of vasopressin activity—demonstrated a high level of maternal care. These findings provide direct evidence for an essential and highly potent role of vasopressin in regulating maternal behaviors, independent of the mother's trait anxiety, according to the authors. — C.A.

"Brain vasopressin is an important regulator of maternal behavior independent of dams' trait anxiety" by Oliver J. Bosch and Inga D. *Neumann* (see pages 17139–17144)